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Intracameral antibiotics to prevent acute endophthalmitis after cataract surgery in Brazil

Antibiótico intracameral para prevenção de endoftalmite aguda pós-cirurgia de catarata no Brasil

Antibiótico intracameral para prevención de endoftalmitis aguda post-cirugía de cataratas en Brasil

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ABSTRACT

Acute endophthalmitis is a serious complication of cataract surgery that, given its infectious etiology, can be prevented using antiseptics and antibiotics. Various drugs and different formulations and routes of administration have been tested for this purpose; however, thus far, besides the well-established preoperative topical application of povidone-iodine, the use of intracameral cefuroxime at the end of surgery is the most effective measure to prevent acute endophthalmitis. However, in Brazil, as in the United States, cefuroxime is not available for intraocular use. This necessitates a search for feasible alternatives to reduce the incidence of this serious surgical complication.

Keywords:
Endophthalmitis;
Cataract;
Antibiotic Prophylaxis;
Cefuroxime

RESUMO

A endoftalmite aguda pós-cirurgia de catarata é uma grave complicação cirúrgica e por ser de etiologia infecciosa pode ser prevenida pelo uso de antissépticos e antibióticos. Diversas drogas e diferentes formas de administração foram testadas com esse fim, entretanto o que se sabe até o momento, é que além do uso tópico já consagrado da iodopovidona pré-operatória, o uso da cefuroxima intracameral ao final da cirurgia é a medida mais eficaz para prevenção da endoftalmite aguda. Todavia no Brasil, assim como nos Estados Unidos, esta droga não se encontra disponível para uso intraocular, o que nos faz buscar alternativas viáveis para diminuir esta grave complicação cirúrgica.

Palavras-Chave:
Endoftalmite;
Catarata;
Antibioticoprofilaxia;
Cefuroxima

RESUMEN

La endoftalmitis aguda post-cirugía de cataratas es una grave complicación quirúrgica y, por ser de etiología infecciosa, se puede prevenir mediante el uso de antisépticos y antibióticos. Diferentes drogas y maneras de administración se han probado con esa finalidad, sin embargo, lo que se sabe hasta el momento es que además del uso tópico ya consagrado de la yodopovidona preoperatoria, el uso de la cefuroxima intracameral al término de la cirugía es la medida más eficaz para prevención de la endoftalmitis aguda. Aún en Brasil, así como en Estados Unidos, dicha droga no se encuentra disponible para uso intraocular, lo que nos hace buscar opciones viables para reducir esa grave complicación quirúrgica.

Palabras Clave:
Endoftalmitis;
Catarata;
Prolaxis Antibiótica;
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INTRODUCTION

Although infrequent, acute endophthalmitis is one of the most feared postoperative complications of cataract surgery. The incidence of this surgical complication varies widely between different continents or countries, and even between neighboring cities. A 2010 study reports an incidence of 0.30% in Brazil,[1] whereas another study from 2013 reports a frequency of 0.03% in Sweden.[2] Acute postoperative endophthalmitis is an extremely serious infectious condition, caused by microorganisms (usually bacteria) introduced into the eye intra- or postoperatively, that can cause irreversible blindness. Some Gram-positive bacteria that most frequently cause acute endophthalmitis after cataract surgery include Staphylococcus epidermidis, S. aureus, β hemolytic *Streptococcus*, and *Enterococcus faecalis*; Gram-negative bacteria include *Haemophilus influenzae* and *Pseudomonas aeruginosa*.[14,19,20] In rare cases, fungi and atypical or anaerobic bacteria cause acute endophthalmitis. A European multicenter study showed that approximately 17% of patients with endophthalmitis subsequently had visual acuity <20/200, whereas 48.3% continued to have visual acuity <20/40.[3] Being an infectious condition, acute endophthalmitis can be prevented with prophylactic antiseptics and antibiotics.

Intracameral Antibiotics

The European Society of Cataract and Refractive Surgeons (ESCRS) published results of its multicenter clinical trial in 2007,[3] demonstrating the benefit of intracameral broad-spectrum antibiotics in the prevention of postoperative endophthalmitis. That study concluded that the use of intracameral cefuroxime significantly reduced (4.92 times) the risk of acute endophthalmitis after cataract surgery, preventing 2 to 4 cases in every 1,000 operated patients, and, thus, it became an important milestone in ophthalmology. A 2013 systematic review and a 2015 meta-analysis have confirmed the relevance of that study, contributing to the adoption of intracameral cefuroxime by numerous surgeons, particularly in Europe.[4,5]

Until 2012, the intracameral solution was constituted by diluting an intravenous preparation of cefuroxime in balanced saline, within the operating room. In 2012, cefuroxime for intracameral use (Aprokam) was approved by the European Medicines Agency (EMA), and was marketed in more than 16 European countries, enabling an even greater number of surgeons to routinely adopt this practice in their surgical procedures.[16,21]

However, in countries such as Brazil and the United States, intracameral cefuroxime (Aprokam) is not available. Therefore, intracameral prophylaxis is adopted only on a small scale in these countries. In 2010, the American Society of Cataract and Refractive Surgeons (ASCRS) conducted a survey[16] which showed that, of the surgeons who responded to the questionnaire, 82% would probably use intracameral antibiotics if they were commercially available. The need to prepare and dilute the drug in the operating room potentially facilitates dilution errors and contamination of the drug that is to be injected into the patient's eye, with a risk of intraocular toxicity (e.g., corneal decompensation and vascular occlusions), which proves a deterrent for surgeons who would otherwise use it.

Alternatives to Cefuroxime

In view of the unavailability of intracameral cefuroxime outside Europe, other antibiotics have been tested for the prophylaxis of endophthalmitis. Vancomycin is highly effective against Gram-positive bacteria, but is essentially ineffective against Gram-negative bacteria; therefore, it should be reserved for infection caused by resistant Gram-positive bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA). Moreover, cases of intraocular toxicity have been reported in patients who received intracameral vancomycin.[22,23]

Recently, moxifloxacin has emerged as an option for the prophylaxis of endophthalmitis. Moxifloxacin is a fourth-generation quinolone with broad-spectrum coverage against Gram-positive and Gram-negative bacteria as well as atypical and anaerobic microorganisms. With pH 6.8 and osmolarity 290 mOsm/kg, it is compatible with intraocular tissues. Animal model studies [6,7] did not find evidence of intraocular toxicity with moxifloxacin use in rabbits. Several retrospective studies[8,9,10,11,13] have concluded that the intracameral use of moxifloxacin in humans is safe and effective for reducing the risk of endophthalmitis. In a recent publication, Haripryia[15] showed an approximately 4-fold reduction in the incidence of endophthalmitis in patients who received an intracameral dose of moxifloxacin.

Lira et al. [24] studied the safety of intracameral moxifloxacin 2 years after cataract surgery. The study included the last 150 surgeries before, and the first after, the introduction of intracameral moxifloxacin (150 μg/0.03 mL) for the prevention of postoperative

endophthalmitis. There were no significant differences between the groups with regard to corneal endothelial cell count, pachymetry, intraocular pressure, or corrected visual acuity. Neither were any ocular or systemic adverse events observed that were associated with the intracameral use of moxifloxacin. Thus far, there have been no randomized prospective studies to test the effectiveness of moxifloxacin, whereas it has been clearly established, by the 2007 ESCRS study, that cefuroxime is both safe and effective when injected into the anterior chamber, for the prevention of endophthalmitis after cataract surgery.[12,14]

Cefuroxime vs Moxifloxacin

Considering the spectrum of activity of both drugs, there is no evidence to date that intracameral moxifloxacin is more effective than cefuroxime in eradicating microorganisms that most frequently cause endophthalmitis. Moreover, the dose of moxifloxacin described in the literature for intracameral use varies from 100 to 500 µg,[8,9,10,11,12] whereas it is well established that the intracameral dose of cefuroxime is 1 mg.[3]

Analyzing the commercial availability of both drugs, specifically in Brazil, the same problem is encountered with both: neither cefuroxime nor moxifloxacin is commercially available for intracameral use. Some surgeons report using a 0.5% ophthalmic solution of moxifloxacin (Vigamox) for prophylactic intracameral use, aspirating the solution to be injected from the eye-drop flask. This practice may raise medicolegal concerns, as the formulation is intended solely for topical use.

In our practice, however, although no drug option for intracameral use has become available, many surgeons choose to use topical antibiotics for prophylaxis. The real effect of the use of antibiotic eye drops, days or hours before the surgical procedure, is controversial. A Swedish study[2] concluded that the pre- and postoperative use of topical antibiotics showed no benefit when compared to chlorhexidine 0.05% and intracameral cefuroxime. A study by He et al. [17] did not find a significant reduction of conjunctival flora after using fourth-generation quinolones either 3 days or 1 day preoperatively. Moss et al. [18] found no statistically significant difference between eyes that received a fourth-generation quinolone 3 days before the procedure and those that received only preoperative povidone-iodine. These findings support the conclusion of the 2007 ESCRS clinical trial that the use of pre- and postoperative antibiotic eye drops offers no benefit when compared to the group injected with intracameral cefuroxime, and, counterproductively, can induce bacterial resistance.

CONCLUSIONS

In this scenario, Brazilian cataract surgeons are in a peculiar situation: there is enough scientific evidence to demonstrate that the use of intracameral cefuroxime is extremely beneficial, yet there is no access to the drug for this particular purpose in this region. In relation to moxifloxacin, the currently available literature suggests that its use reduces the risk of endophthalmitis, but because the studies are retrospective, their evidence is inferior to that of controlled and randomized clinical trials. Furthermore, because we do not have access to the drug for intraocular use, it is not possible for us to use it for that purpose with the requisite legal support. Meanwhile, we wait for cefuroxime to be marketed for intracameral use in Brazil, and for new studies to be conducted with a greater level of scientific evidence that would authorize the intracameral use of other drugs.

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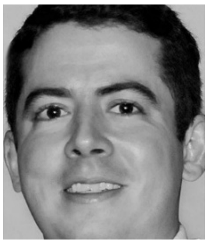
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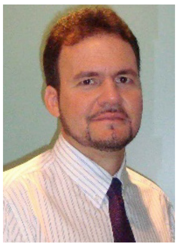
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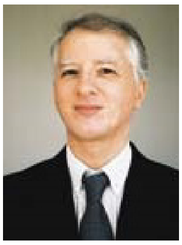
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